PATENT COOPERATION TREA

From the INTERNATIONAL SEARCHING AUTHORITY

LJH

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT AND THE WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY, OR THE DECLARATION

(PCT Rule 44.1)

To:
TOWNSEND AND TOWNSEND AND CREW LLP
Attn. Hyman, Laurence J.
Two Embarcadero Center
8th floor
San Francisco, CA 94111-3834
UNITED STATES OF AMERICA

015280-485100 PC

Applicant's or agent's file reference 15280-4851PC	**FOR FURTHER ACTION** See paragraphs 1 and 4 below
International application No. PCT/US2004/041639	International filing date *(day/month/year)* 13/12/2004
Applicant THE GOVERNMENT OF THE UNITED STATES, AS	

Date of mailing *(day/month/year)* 31/08/2005

1. [x] The applicant is hereby notified that the international search report and the written opinion of the International Searching Authority have been established and are transmitted herewith.

   Filing of amendments and statement under Article 19: 10/31/05
   The applicant is entitled, if he so wishes, to amend the claims of the International Application (see Rule 46):

   When? The time limit for filing such amendments is normally 2 months from the date of transmittal of the International Search Report; however, for more details, see the notes on the accompanying sheet.

   Where? Directly to the International Bureau of WIPO, 34 chemin des Colombettes 1211 Geneva 20, Switzerland, Fascimile No.: (41-22) 740.14.35

   For more detailed instructions, see the notes on the accompanying sheet.

2. [ ] The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect and the written opinion of the International Searching Authority are transmitted herewith.

3. [ ] **With regard to the protest** against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

   [ ] the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.

   [ ] no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Reminders** 4/1/05

   Shortly after the expiration of **18 months** from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in Rules 90*bis*.1 and 90*bis*.3, respectively, before the completion of the technical preparations for international publication.

   The applicant may submit comments on an informal basis on the written opinion of the International Searching Authority to the International Bureau. The International Bureau will send a copy of such comments to all designated Offices unless an international preliminary examination report has been or is to be established. These comments would also be made available to the public but not before the expiration of 30 months from the priority date.

   Within **19 months** from the priority date, but only in respect of some designated Offices, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until **30 months** from the priority date (in some Offices even later); otherwise, the applicant must, **within 20 months** from the priority date, perform the prescribed acts for entry into the national phase before those designated Offices. 4/12/06 8/12/05

   In respect of other designated Offices, the time limit of **30 months** (or later) will apply even if no demand is filed within 19 months.

   See the Annex to Form PCT/IB/301 and, for details about the applicable time limits, Office by Office, see the *PCT Applicant's Guide*, Volume II, National Chapters and the WIPO Internet site.

Name and mailing address of the International Searching Authority European Patent Office, P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Authorized officer Anu Evers art 19 amendment DOCKETED BY

Form PCT/ISA/220 (January 2004) (See notes on accompanying sheet)

search rept rcvd
DOCKETED BY

file IDS
DOCKETED BY

PATENT COOPERATION TREA

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference	**FOR FURTHER ACTION**	see Form PCT/ISA/220 as well as, where applicable, item 5 below.
15280-4851PC		
International application No.	International filing date *(day/month/year)*	(Earliest) Priority Date *(day/month/year)*
PCT/US2004/041639	13/12/2004	12/12/2003
Applicant		
THE GOVERNMENT OF THE UNITED STATES, AS		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 8 sheets.

[X] It is also accompanied by a copy of each prior art document cited in this report.

1. **Basis of the report**
   a. With regard to the **language,** the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
      [ ] The international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).
   b. [ ] With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, see Box No. I.

2. [X] **Certain claims were found unsearchable** (See Box II).

3. [ ] **Unity of invention is lacking** (see Box III).

4. With regard to the **title,**
   [ ] the text is approved as submitted by the applicant.
   [X] the text has been established by this Authority to read as follows:
   IMMUNOGENIC PEPTIDE FRAGMENTS OF XAGE-1

5. With regard to the **abstract,**
   [X] the text is approved as submitted by the applicant.
   [ ] the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box No. IV. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. With regard to the **drawings,**
   a. the figure of the **drawings** to be published with the abstract is Figure No. _____
      [ ] as suggested by the applicant.
      [ ] as selected by this Authority, because the applicant failed to suggest a figure.
      [ ] as selected by this Authority, because this figure better characterizes the invention.
   b. [X] none of the figures is to be published with the abstract.

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US2004/041639

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 C07K14/47 A61K38/17 A61P35/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
EPO-Internal, WPI Data, PAJ, CHEM ABS Data, Sequence Search

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/037267 A (CORIXA CORPORATION; HENDERSON, ROBERT, A; WANG, TONGTONG; WATANABE, YO) 8 May 2003 (2003-05-08) page 5, line 3 - page 7, line 28; claims 4-6,13-15; example 25; sequence 1943	1-74
X	WO 02/18584 A (THE GOVERNMENT OF THE UNITED STATES, AS REPRESENTED BY THE SECRETARY O) 7 March 2002 (2002-03-07) cited in the application abstract; page 5, last paragraph; paragraph joining pages 23 and 24; paragraph joining pages 30 and 31; page 31, last paragraph; figure 1	46-64, 73,74
X	WO 01/46696 A (ABBOTT LABORATORIES) 28 June 2001 (2001-06-28) claims 28,37-39,43; sequence 173	66

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 July 2005	31/08/2005

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Fausti, S

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Form PCT/ISA/210 (second sheet) (January 2004)

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 03/053332 A (MYRIAD GENETICS, INC; MORHAM, SCOTT; ZAVITZ, KENTON; HOBDEN, ADRIAN) 3 July 2003 (2003-07-03) page 84 - page 85; table 18; sequence 3476	66
X	WO 00/70044 A (THE JOHNS HOPKINS UNIVERSITY; MITTMAN, SCOTT; AGNEW, WILLIAM, S) 23 November 2000 (2000-11-23) page 22; sequences 35,116	66,68
X	WO 99/61467 A (MCGILL UNIVERSITY; TREMBLAY, MICHEL, L; COTE, JEAN-FRANCOIS; ANGERS-LO) 2 December 1999 (1999-12-02) page 35, second paragraph; figure 18a, peptide P369A	66,68
X	WO 01/59063 A2 (HUMAN GENOME SCIENCES, INC., USA) 16 August 2001 (2001-08-16) abstract; sequence 3473 -& DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; ROSEN, CRAIG A. ET AL: "Nucleic acids and their encoded polypeptides from human nervous system" XP002335800 retrieved from STN Database accession no. 135:328137 abstract	66,68
X	WO 03/033515 A1 (CORIXA CORPORATION, USA) 24 April 2003 (2003-04-24) abstract; sequence 28097 -& DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; MITCHAM, JENNIFER L. ET AL: "Propionibacterium acnes genes and encoded protein sequences and their use in therapy and diagnosis of acne vulgaris" XP002335801 retrieved from STN Database accession no. 138:298928 abstract	66,68
X	JOURNAL OF VIROLOGY, vol. 68, no. 11, 1994, pages 7620-7627, XP009050647 ISSN: 0022-538X abstract; figure 2	66
X	US 2003/194704 A1 (PENN, SHARRON GAYNOR ET AL) 16 October 2003 (2003-10-16) abstract; sequence 28051	66,68

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-& DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; PENN, SHARRON GAYNOR ET AL: "Human genome-derived single exon nucleic acid probes useful for analysis of gene expression in human tissues" XP002335804 retrieved from STN Database accession no. 139:303032 abstract	
X	WO 01/71042 A2 (PE CORPORATION , USA) 27 September 2001 (2001-09-27) abstract; sequence 37059 -& DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; VENTER, J. CRAIG ET AL: "Reagents and kits, such as nucleic acid arrays, for detecting the expression of over 10,000 Drosophila genes" XP002335805 retrieved from STN Database accession no. 136:396933 abstract	66,68
X	PEREZ-PAYA, ENRIQUE ET AL: "Functionalized protein-like structures from conformationally defined synthetic combinatorial libraries" JOURNAL OF BIOLOGICAL CHEMISTRY , 271(8), 4120-6 CODEN: JBCHA3; ISSN: 0021-9258, 1996, XP002335724 abstract; table IV	68
P,X	CHEN CHUNG-YUNG ET AL: "Comparative genome analysis of Vibrio vulnificus, a marine pathogen." GENOME RESEARCH. DEC 2003, vol. 13, no. 12, December 2003 (2003-12), pages 2577-2587, XP002335772 ISSN: 1088-9051 abstract -& DATABASE UniProt 'Online! "Hypothetical protein VV0919" 1 March 2004 (2004-03-01), XP002335806 retrieved from EBI accession no. UNIPROT-Q7MMZ8 Database accession no. Q7MMZ8 Sequence of protein VV0919	66,68
P,X	US 2004/214272 A1 (LA ROSA, THOMAS J. ET AL) 28 October 2004 (2004-10-28) abstract; sequence 228482 -/--	66,68

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
	-& DATABASE CA 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; LA ROSA, THOMAS J. ET AL: "Nucleic acid molecules and encoded proteins associated with maize and their uses for plant improvement" XP002335807 retrieved from STN Database accession no. 142:18505 abstract -----	

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2004/041639

Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. [X] Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 21-27, 40-65 and 70-74 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

2. [ ] Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

3. [ ] Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. [ ] As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.

2. [ ] As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.

3. [ ] As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:

4. [ ] No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

[ ] The additional search fees were accompanied by the applicant's protest.

[ ] No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No
PCT/US2004/041639

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 03037267 A	08-05-2003	US 2003054363 A1	20-03-2003
		US 2003170255 A1	11-09-2003
		CA 2465183 A1	08-05-2003
		EP 1446013 A2	18-08-2004
		WO 03037267 A2	08-05-2003
		US 2003211510 A1	13-11-2003
WO 0218584 A	07-03-2002	AU 8700401 A	13-03-2002
		WO 0218584 A2	07-03-2002
WO 0146696 A	28-06-2001	US 2003049601 A1	13-03-2003
		CA 2393500 A1	28-06-2001
		EP 1247099 A2	09-10-2002
		JP 2003525428 T	26-08-2003
		WO 0146696 A2	28-06-2001
		US 2003211467 A1	13-11-2003
WO 03053332 A	03-07-2003	AU 2002324753 A1	09-07-2003
		WO 03053332 A2	03-07-2003
		US 2003171318 A1	11-09-2003
		US 2004109861 A1	10-06-2004
WO 0070044 A	23-11-2000	AU 4989500 A	05-12-2000
		WO 0070044 A2	23-11-2000
WO 9961467 A	02-12-1999	AU 3922999 A	13-12-1999
		CA 2329157 A1	02-12-1999
		WO 9961467 A2	02-12-1999
		EP 1077997 A2	28-02-2001
		JP 2002516338 T	04-06-2002
		AU 1543600 A	03-07-2000
		CA 2353997 A1	22-06-2000
		WO 0036111 A1	22-06-2000
		EP 1137780 A1	04-10-2001
		JP 2002532515 T	02-10-2002
		US 6534056 B1	18-03-2003
WO 0159063 A2	16-08-2001	AU 2950801 A	07-08-2001
		AU 3095801 A	07-08-2001
		AU 3645901 A	07-08-2001
		AU 3646001 A	07-08-2001
		AU 3646101 A	07-08-2001
		AU 3646201 A	07-08-2001
		AU 3646301 A	07-08-2001
		AU 3646401 A	07-08-2001
		AU 3646501 A	07-08-2001
		AU 3646601 A	07-08-2001
		AU 3794301 A	07-08-2001
		AU 3794401 A	07-08-2001
		AU 3794701 A	07-08-2001
		AU 3794901 A	07-08-2001
		AU 3795001 A	07-08-2001
		AU 3795101 A	07-08-2001
		AU 3795201 A	07-08-2001
		AU 3795301 A	07-08-2001
		AU 3795401 A	07-08-2001
		AU 3795501 A	07-08-2001
		AU 3795701 A	07-08-2001

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 0159063 A2		AU 3795801 A	07-08-2001
		AU 3972601 A	07-08-2001
		AU 3972701 A	07-08-2001
		AU 3972801 A	07-08-2001
		AU 4140201 A	07-08-2001
		AU 4140301 A	07-08-2001
		AU 4140401 A	07-08-2001
		AU 4140501 A	07-08-2001
		AU 4140601 A	07-08-2001
		AU 4140701 A	07-08-2001
		AU 4140801 A	07-08-2001
		AU 4140901 A	07-08-2001
		AU 4141001 A	07-08-2001
		AU 4141101 A	20-08-2001
		AU 4141201 A	07-08-2001
		AU 4141301 A	07-08-2001
		AU 4141401 A	07-08-2001
		AU 4141501 A	07-08-2001
		AU 4141601 A	07-08-2001
		AU 4141701 A	07-08-2001
		AU 4141801 A	07-08-2001
		AU 4141901 A	07-08-2001
		AU 4313401 A	07-08-2001
		AU 4313501 A	07-08-2001
		AU 4313601 A	07-08-2001
		AU 4313701 A	14-08-2001
		AU 4526201 A	07-08-2001
		AU 4719001 A	07-08-2001
		AU 4719101 A	07-08-2001
WO 03033515 A1	24-04-2003	NONE	
US 2003194704 A1	16-10-2003	GB 2387601 A	22-10-2003
WO 0171042 A2	27-09-2001	AU 4594501 A	03-10-2001
US 2004214272 A1	28-10-2004	US 2004216190 A1	28-10-2004

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

LJH PCT

To:

see form PCT/ISA/220

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

015280-485100PC

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

FOR FURTHER ACTION
See paragraph 2 below 11/30/05

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/US2004/041639	13.12.2004	12.12.2003

International Patent Classification (IPC) or both national classification and IPC
C07K14/47, A61K38/17, A61P35/00

Applicant
THE GOVERNMENT OF THE UNITED STATES, AS .....

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later. 11/30/05 10/12/05

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:

European Patent Office
D-80298 Munich
Tel. +49 89 2399 - 0 Tx: 523656 epmu d
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Authorized Officer

Fausti, S

Telephone No. +49 89 2399-7389

response to written opinion
DOCKETED BY

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/US2004/041639

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

Box No. II Priority

1. ☒ The validity of the priority claim has not been considered because the International Searching Authority does not have in its possession a copy of the earlier application whose priority has been claimed or, where required, a translation of that earlier application. This opinion has nevertheless been established on the assumption that the relevant date (Rules 43*bis*.1 and 64.1) is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

   see separate sheet

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 21-27,40-65,70-74 (with respect to Industrial Applicability)

because:

☒ the said international application, or the said claims Nos. 21-27,40-65,70-74 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the whole application or for said claims Nos.

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See separate sheet for further details

Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	-
	No:	Claims	1-74
Inventive step (IS)	Yes:	Claims	-
	No:	Claims	1-74
Industrial applicability (IA)	Yes:	Claims	1-20,28-39,66-69
	No:	Claims	-

2. Citations and explanations

see separate sheet

Box No. VI Certain documents cited

1. Certain published documents (Rules 43*bis*.1 and 70.10)

and / or

2. Non-written disclosures (Rules 43*bis*.1 and 70.9)

see form 210

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item II

Priority

P.1 For the purpose of this examination, the priority date is considered to be valid. Hence, the disclosure of the Vibrio vulnificus protein containing the peptide motif VSPSAPSL is not considered to be part of the state of the art (Rule 64 PCT). It appears that the amino acid sequence of this protein has been made available to the public on the first of March 2004, after the relevant priority date. This amino acid sequence is not disclosed in the serial publication (see document D13 and point 1.13 below). Similarly, D14 is not considered prior art (see point 1.14 and I.1 below).

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

N.1 Claims 21-27, 40-65 and 70-74 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. DOCUMENTS.

Reference is made to the following documents:

D1: WO 03/037267 A;
D2: WO 02/18584 A;
D3: WO 01/46696 A;
D4: WO 03/053332 A;

D5: WO 00/70044 A;
D6: WO 99/61467 A;
D7: WO 01/59063 A;
D8: WO 03/033515 A;
D9: Tobin G. J. et Al., *Journal of Virology* (1994), Vol. 68, No. 11, Pages 7620-7627;
D10: US 2003/194704 A;
D11: WO 01/71042 A;
D12: Perez-paya E. Et Al., *Journal of Biological Chemistry* (1996) Vol. 271, No. 8, Pages 4120-4126;
D13: Chen Chung-yung Et Al., *Genome Research* (2003) Vol. 13, No. 12, 2577-2587;
D14: US 2004/214272 A.

1.1 D1 discloses immunogenic peptides for use in cancer immunotherapy (see the abstract and lines 3-16 on page 5). In particular, these peptides elicit immune responses in the patient, e.g. by stimulating and/or expanding T-cells, eventually through peptide-specific antigen presenting cells (see lines 3-28 on page 7). The preferred peptides are epitopes of XAGE-1 and are the targets for vaccine and other immunotherapeutic approaches (see example 25). In particular, one of these epitopes is a peptide of 20 amino acid residues containing the motif GVFPSAPSPV (see Seq. ID 1943). D1 discloses polynucleotides, vectors and host cells encoding/expressing this specific XAGE-1 epitope, as well as the corresponding pharmaceutical compositions and methods of cancer immunotherapy involving them (see claims 4-6 and 13-15).

1.2 D2 discloses the two translated forms of XAGE-1, namely p9 and p16, and their amino acid sequence (see the abstract and figure 1). D2 teaches that these proteins, immunogenic fragments thereof, the corresponding encoding polynucleotides and expression vectors are useful in the treatment of XAGE-1 expressing cancers, as they elicit an immune, e.g. T-cell, response to the cancer cells (see the abstract, the last paragraph on page 5 and the paragraph joining pages 30 and 31). The preferred peptide fragments are from 5 to 15 amino acid residues in length (see the paragraph joining pages 23 and 24). In addition, D2 discloses immunoconjugates comprising an anti-p9 or anti-p16 antibody and toxic or labelling moieties for inhibiting the growth of

XAGE-1 expressing cells or for diagnostic purposes (see again the abstract).

1.3 D3 discloses an immunogenic peptide of 33 amino acid residues containing the motif TSPSAPPL as a peptide vaccine against the hepatitis E virus (see: abstract; claims 28 and 39; Seq. ID 173).

1.4 D4 discloses viral peptide fragments, which inhibit viral budding, for the treatment of viral infections (see the abstract). In particular, D4 discloses peptides of 9-20 amino acid residues from the Colorado Tick Fever Virus VP12 containing the motif VAPSAPSA (see table 18 on pages 84 and 85).

1.5 D5 discloses a protein-coding exon from the calcium channel α-II subunit gene, which corresponds to a peptide of 48 amino acid residues containing the motif AFPSAPSL (see the "Exon 34" on page 22, Seq. IDs 35 and 116).

1.6 D6 discloses the pallixin binding domain of the protein tyrosine phosphatase PEST and alanine mutants thereof (see figure 18a). In particular, this binding domain is of 20 amino acid residues in length, and one of the alanine mutant contain the sequence LTPSAPSA (see the mutant P369A).

1.7 D7 discloses nervous system antigens and their encoding polynucleotides for diagnosis and treatment of nervous system cancers and metastases (see abstract). One of these antigens is of 50 amino acid residues in length and containing the peptide motif VGPSAPSL (see Seq. ID 3743).

1.8 D8 discloses immunogenic fragments of *Propionibacterium acnes* proteins and their encoding polynucleotides for the treatment of acne (see the abstract). In one specific embodiment, D8 discloses a polypeptide 50 amino acid residues which contains the motif VSPSASPI (see Seq. ID 28097).

1.9 D9 discloses proteolytic cleavage products from the bovine immunodeficiency virus Gag precursor polypeptide (see the title). In particular, D9 discloses a peptide fragment of 18 amino acid residues containing the motif VTPSAPPL (see figure 2).

1.10 D10 discloses single exon nucleic acid probes useful for gene expression analysis (see the abstract). In addition, D10 discloses the peptides encoded by these exons and antibodies against these antigenic peptides (see the abstract). In a specific embodiment, the peptide is of 33 amino acids in length and contains the sequence LLPSAPPL (see Seq. ID 28051).

1.11 D11 discloses nucleic acid sequences from the *Drosophila melanogaster* genome and the predicted transcript polypeptides (see the abstract). In particular, D11 discloses a peptide of 48 amino acids containing the motif APPSAPPT (see Seq. ID 37059).

1.12 D12 discloses combinatorial libraries of synthetic peptides (see the abstract). In a specific embodiment, the library includes a peptide of 18 amino acid residues containing the sequence AAPSASPA (see the line 8 of table IV).

1.13 D13 discloses a protein sequence of 50 amino acid residues from the marine pathogen *Vibrio vulnificus* containing the peptide domain VSPSAPSL (see the Uniprot database entry).

1.14 D14 discloses polypeptides and polynucleotides for the production of transgenic plants (see the abstract). In particular, D14 discloses a polypeptide of 45 amino acid residues containing the motif VSPSAPPT (see Seq. ID 228482).

2. INDUSTRIAL APPLICABILITY (Art. 33(4) PCT).

2.1 For the assessment of the present claims 21-27, 40-65 and 70-74 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

2.2 Claims 1-20, 28-39 and 66-68 relate to immunogenic peptides, nucleic acids encoding these peptides, pharmaceutical compositions and expression vectors containing these peptides/nucleic acids, and their uses in the manufacture of medicaments. These peptides, nucleic acids, compositions, vectors and uses can be made or applied in the pharmaceutical industry, hence they are to be considered industrially applicable according to article 33(4) PCT.

3. NOVELTY (Art. 33(2) PCT) and INVENTIVE STEP (Art. 33(3) PCT).

3.1 The subject-matter of independent claims 1 and 66 is not novel over the immunogenic peptide epitope of XAGE-1, which contains the sequence GVFPSAPSPV and is disclosed in D1 (see point 1.1 above).

3.1[a] Dependent claims 2-7 and claims 8-65, 67-74 do not contain any features which, in combination with the features of any claim to which they refer or in combination with the features of the peptide of claim 1, meet the requirements of the PCT in respect of novelty and/or inventive step, given the disclosure of D1. In particular, D1 specifically teaches and/or suggests the use of this and similar peptides in cancer immunotherapy, as well as the use of the corresponding polynucleotides, expression vectors and antigen presenting cells (see point 1.1 above and particularly the last paragraph of example 25 of D1).

3.2 In addition, the subject-matter of independent claims 46, 57, 63, 73 and 74 lacks novelty over D2, which discloses whole XAGE-1 proteins and polynucleotides for use in cancer immunotherapy (see point 1.2 above), because these claims do not clearly define the sequence length of the claimed peptide (see point C.2 below).

3.2[a] Dependent claims 47-56, 58-62, 64 and 65 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty and/or inventive step, given the disclosure of D2 (see point 1.2 above).

3.3 The subject-matter of claim 66 is not novel over the peptides containing the PSA motif disclosed in any of D3-D12 (see point 1.3-1.12 above). In particular, the peptides of D3, D7, D8 and D10 are antigens or immunogenic fragments thereof. The

claim definition is very broad with respect to the immunogenic properties of the peptide, as the claim generically refers to "immunogenic peptide" without any limiting condition. It is considered that the peptides disclosed in D5-D6, D9 D11 and D12 are inherently immunogenic according to such a broad claim scope in view of their size, e.g. they would be immunogenic under suitable conditions in a foreign organism. Glycine, proline, serine and threonine are neutral, weakly hydrophobic amino acid residues and are therefore to be considered within the suitable hydrophobic residues for the variable X_3. Moreover, the application does not provide a more specific definition of hydrophobic residues.

3.3[a] Claim 68 does not contain any features which, in combination with the features of claim 66, meet the requirements of the PCT in respect of novelty, given the disclosure of this prior art. For example, D5, D7, D8, D10 and D11 disclose polynucleotides encoding the PSA-polypeptides.

Re Item VI
Certain documents cited

Certain published documents (Rule 70.10 PCT).

I.1 It appears that D14 discloses a peptide sequence according to claim 66 (see point 1.14 above).

Re Item VII
Certain defects in the international application

D.1 The expression "*...incorporated by reference...*" (see page 1, line 5) is to be deleted because, only when the matter of the concerning prior art document is essential to satisfy the requirements of Article 5 PCT, this matter should be directly incorporated in the description. Moreover, regarding to the disclosure of the claimed subject-matter, the patent specification should be self-contained (see PCT Guidelines, Section IV, II-4.17).

D.2 Contrary to the requirements of Rule 5.1(a)(ii) PCT, the relevant background art disclosed in the document D1, and eventually in documents D3-D14, is not mentioned in the description, nor is/are this/these document/s identified therein.

Re Item VIII

Certain observations on the international application

C. CLARITY and CONCISENESS (Art. 6 PCT).

C.1 Although claims 40 with 21, claims 46 with 57 and claims 1 with 66 have been drafted as separate independent claims, each of these pairs appears to relate effectively to the same subject-matter and the corresponding paired claims differ from each other only with regard to the definition of the preferred or alternative features of the claimed subject-matter. The aforementioned claims therefore lack conciseness.

C.2 The definition of claims 46 and 57 is unclear with respect to the sequence length of the peptide. The claims do not provide any upper limit for the peptide sequence and do not refer to the amino acid sequence as representing the whole peptide. In the light of dependent claims 50 and 61, the claims are to be interpreted as relating to peptides of 10 or more residues comprising the given amino acid sequence with no upper limit in the number of residues. According to this interpretation, the peptide definition of claims 46 and 57 is equivalent to the one of claims 63, 73 and 74, namely a definition of a peptide of at least 10 amino acid residues without further restriction in the sequence length (see the expression "peptide comprising an amino acid sequence" in claims 63, 73 and 74).

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the PCT Applicant's Guide, a publication of WIPO.

In these Notes, "Article", "Rule", and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international pbulication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended?

Under Article 19, only the claims may be amended.

Dunng the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.

NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped),whether

(i) the claim is unchanged;

(ii) the claim is cancelled;

(iii) the claim is new;

(iv) the claim replaces one or more claims as filed;

(v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers; claims 30, 33 and 36 unchanged; new claims 49 to 51 added."

2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."

3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."

4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international appplication is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the same time of filing the amendments with the International Bureau, also file a copy of such amendments with the International Preliminary Examining Authority (see Rule 62.2(a), first sentence).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, where upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see Volume II of the PCT Applicant's Guide.